

FIGURE 1

cis/trans isomerization of a peptidyl-prolyl bond
(Acetyl-prolyl-N-methylamid)

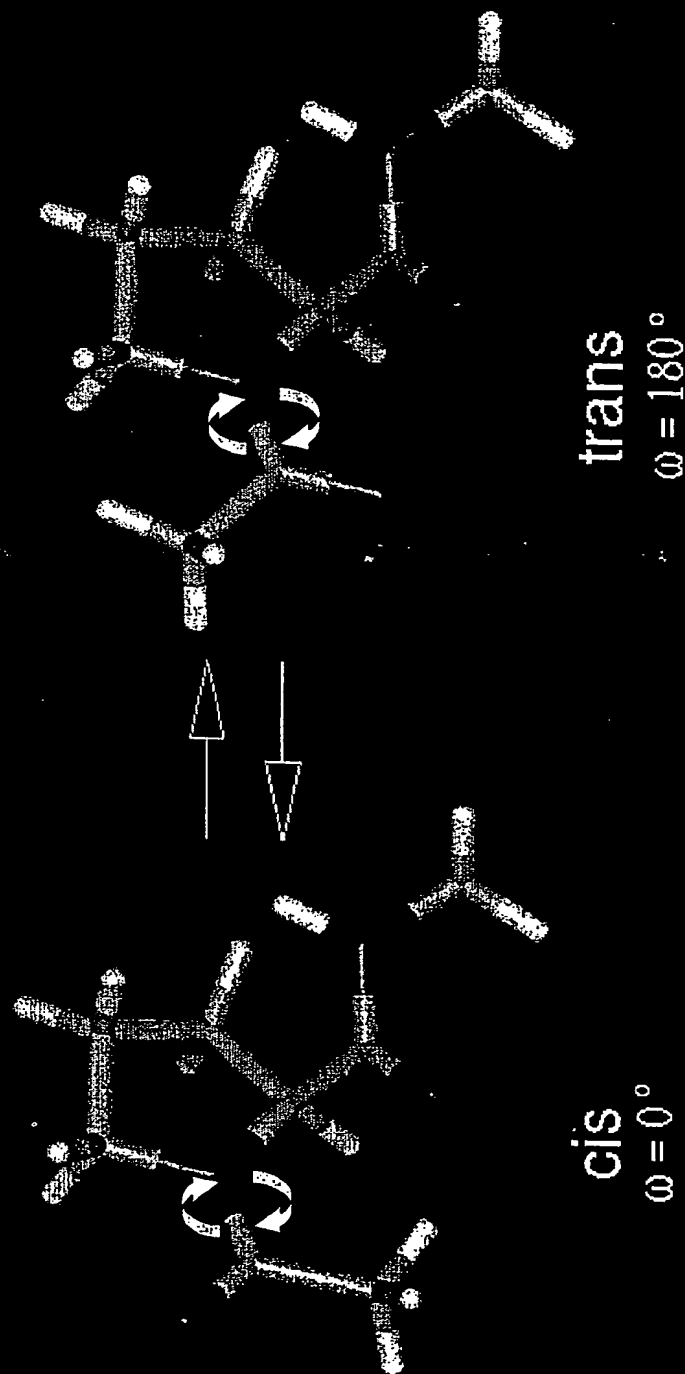
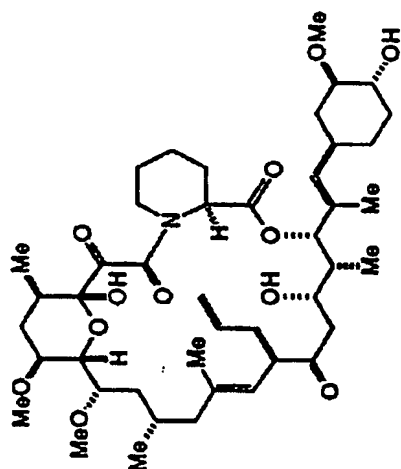
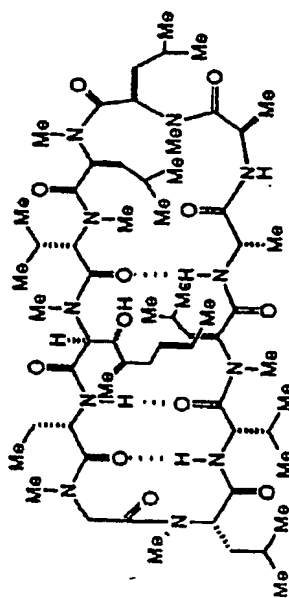


FIGURE 2

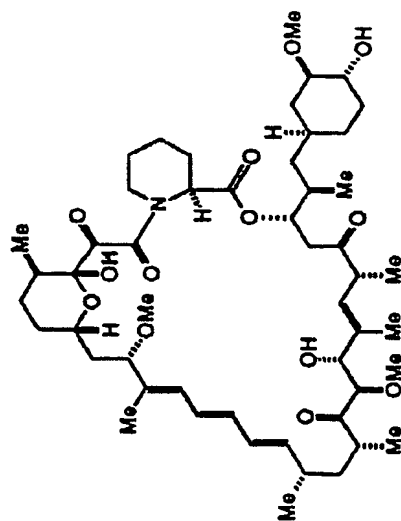
Structure of Immunophilin Ligands



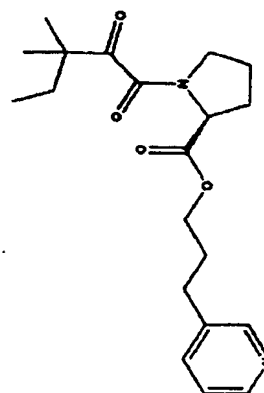
FK506



Cyclosporin A



Rapamycin



GPI-1046

FIGURE 3

Effect of FK-506 on mGluR5 Binding to Homer

Time Course

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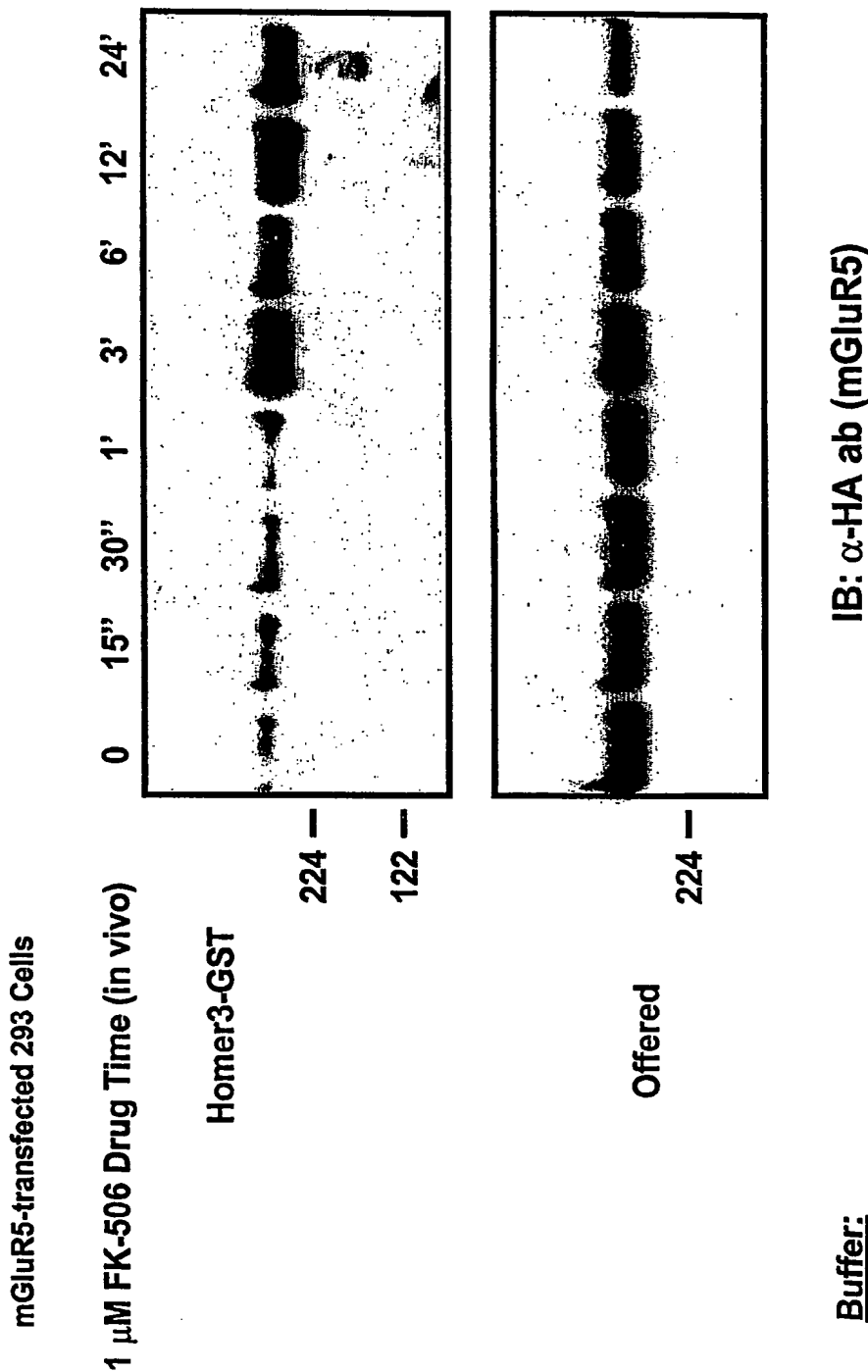


FIGURE 4

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Effect of GPI-1046 on mGluR5 Binding to Homer

Time Course

mGluR5-transfected 293 Cells

1 μ M GPI-1046 Drug Time (in vivo)

0 30" 1' 3' 6' 12' 24'

Homer3-GST

224 —

Offered

224 —

IB: α -HA ab (mGluR5)

Buffer:

1 % TX-100

Calyculin A

NaF, NaPyrophosphate, NaVO3

Protease Inhibitor

FIGURE 5

FKBP52-GST Pulls Down mGluR5

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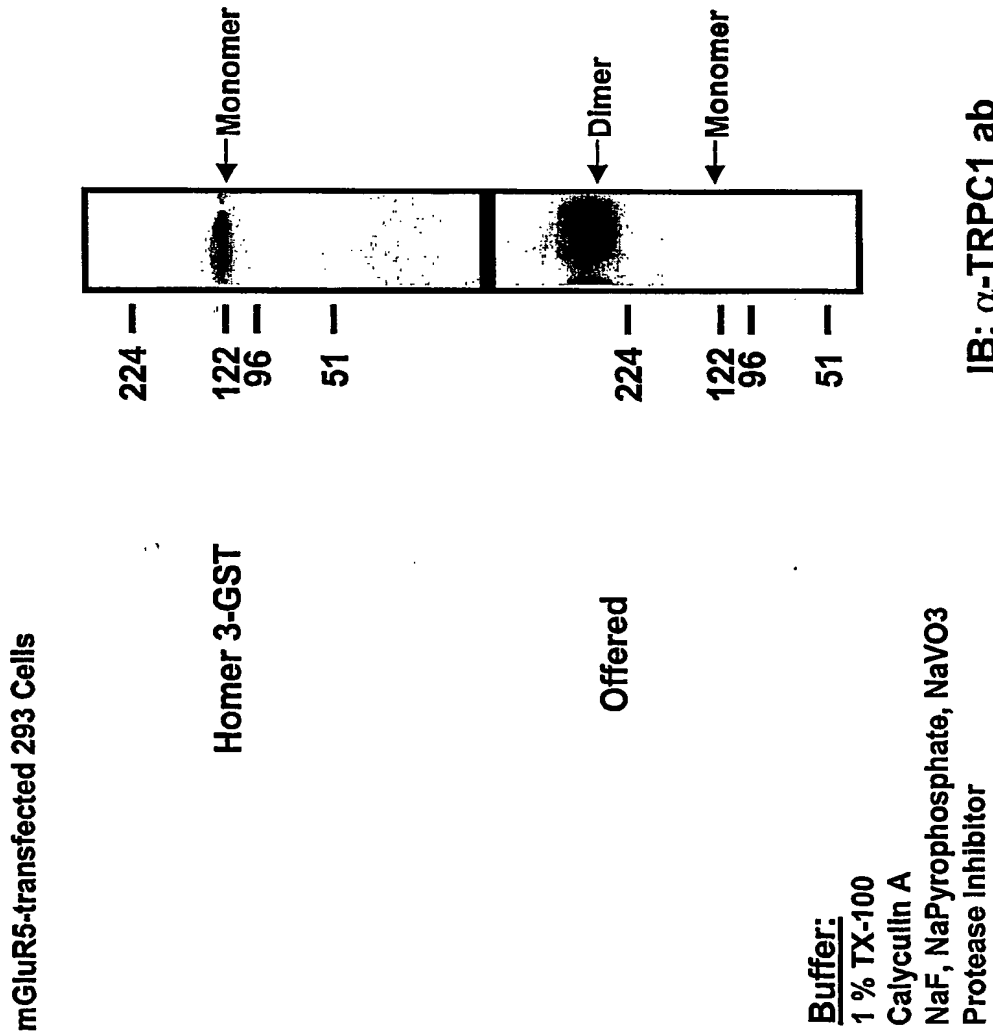


FIGURE 6

Increasing FKBP-12/-52 Increases Homer Binding to mGluR5

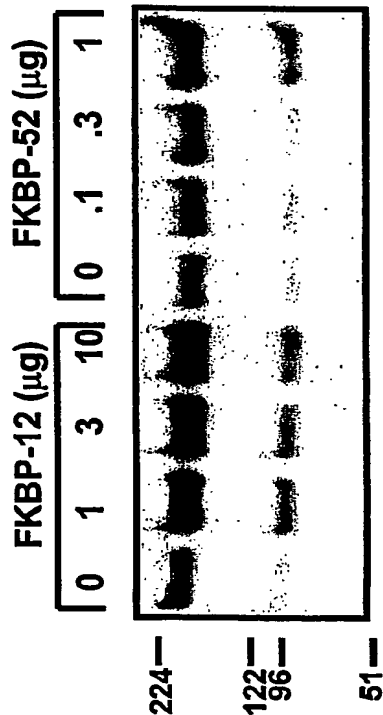
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mGluR5-transfected 293 Cells +:



Homer3-GST

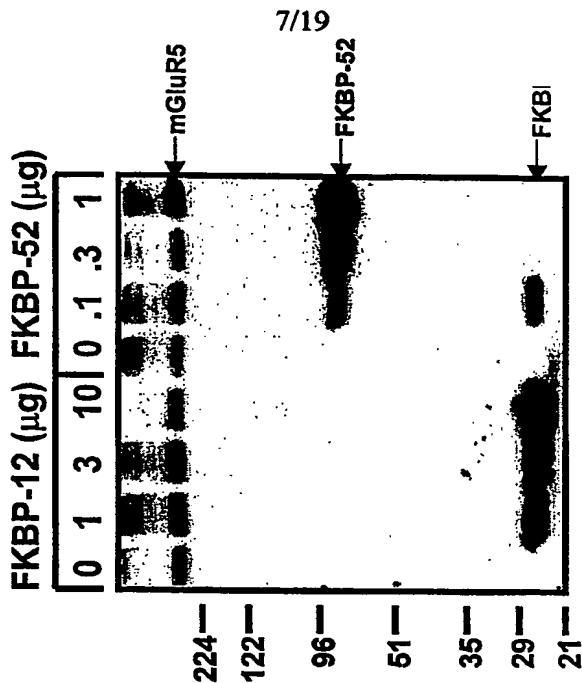
Buffer:

1 % TX-100

Calyculin A

NaF, NaPyrophosphate, NaVO3

Protease Inhibitor



Offered

IB: α-HA ab

FIGURE 7

Phylogenetic Relationship in the TRP Protein Family

Clapham et al., 2001

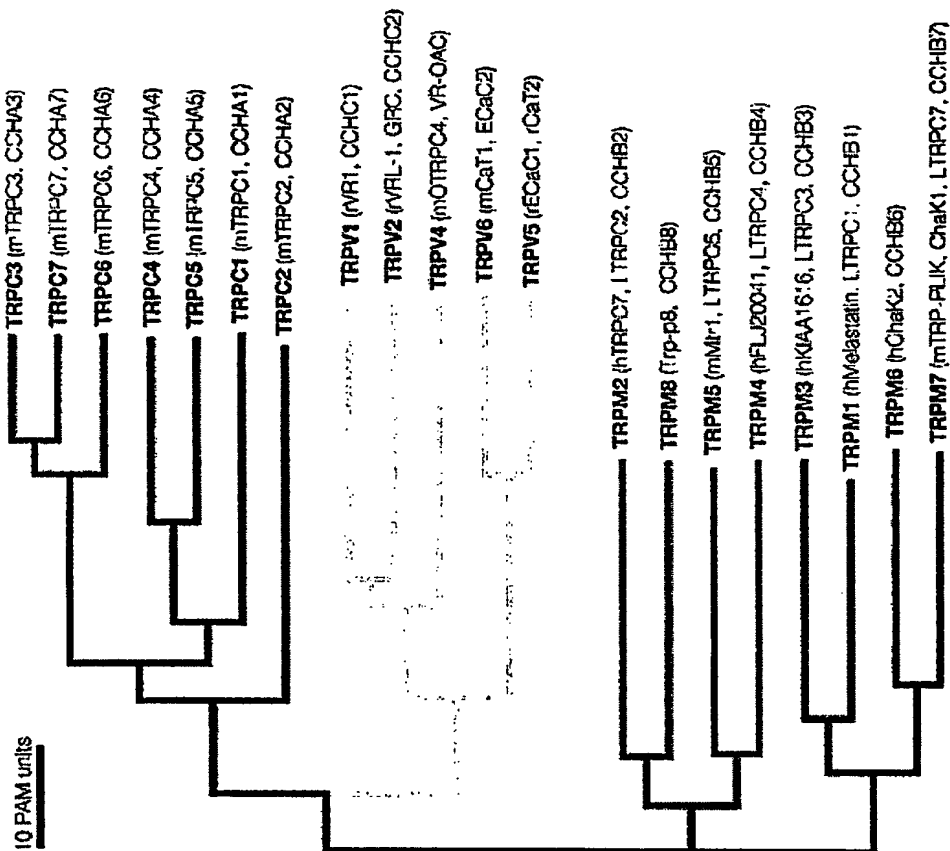
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FIGURE 8

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Amino Acid Sequence of TRPC1 and Alignment to Other TRP

Wes et al., 1995

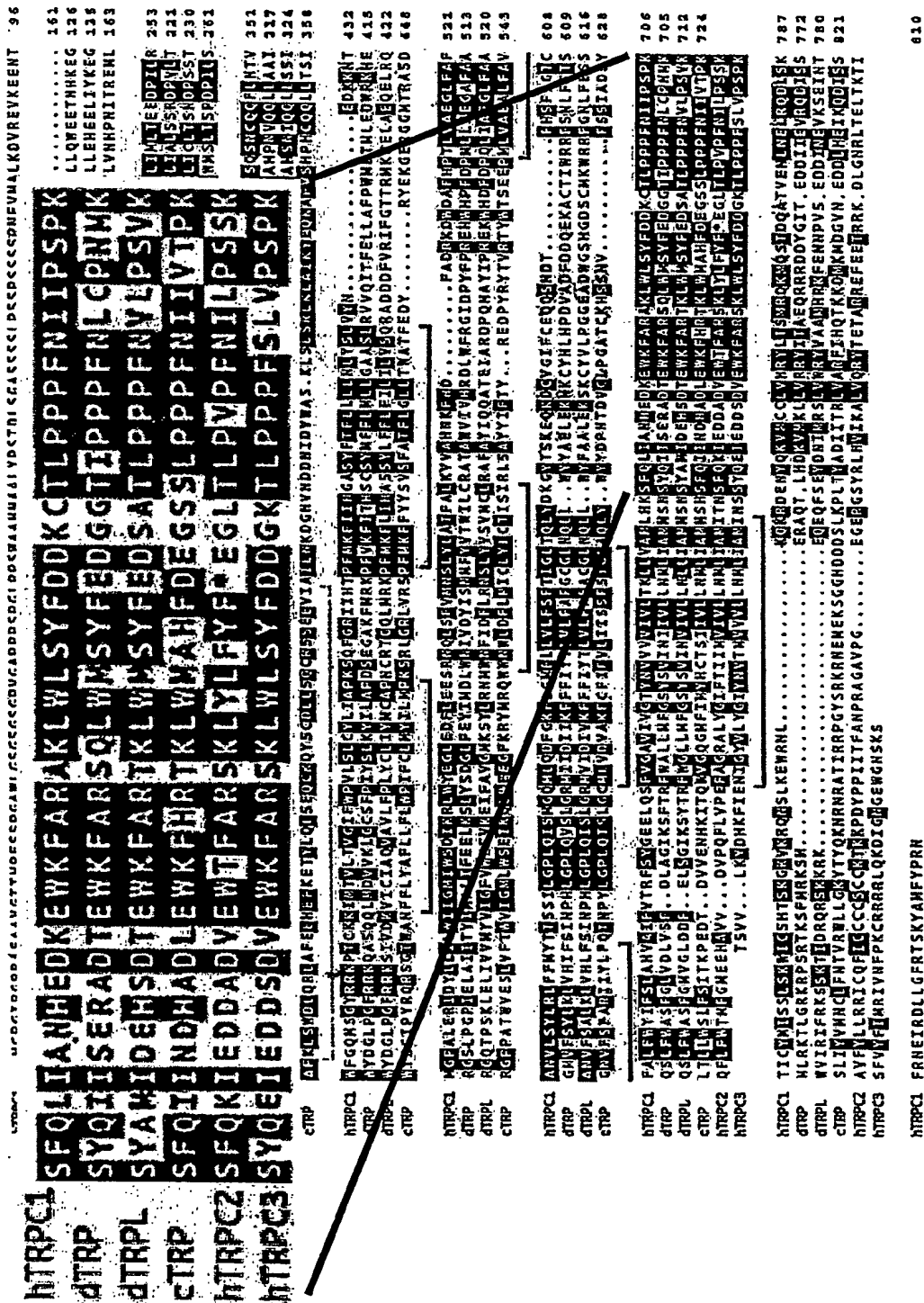
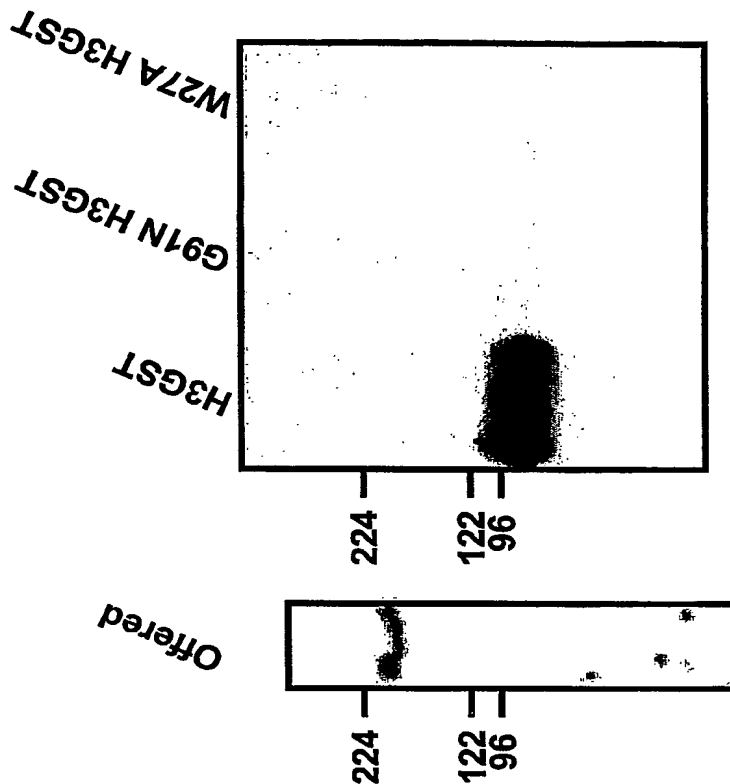


FIGURE 9

Homer 3-GST Pulls Down TRPC1 from Cerebellum

Solubilized in 1 % TX-100
 37,000 x g Spin



Buffer:
 Calyculin A
 NaF, NaPyrophosphate, NaVO3
 Protease Inhibitor

IB: α -TRPC1 ab

FIGURE 10

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Brain Co-IP of Homer and TRPC1

IP: α -Homer 1 ab



Hippocampus

Buffer:

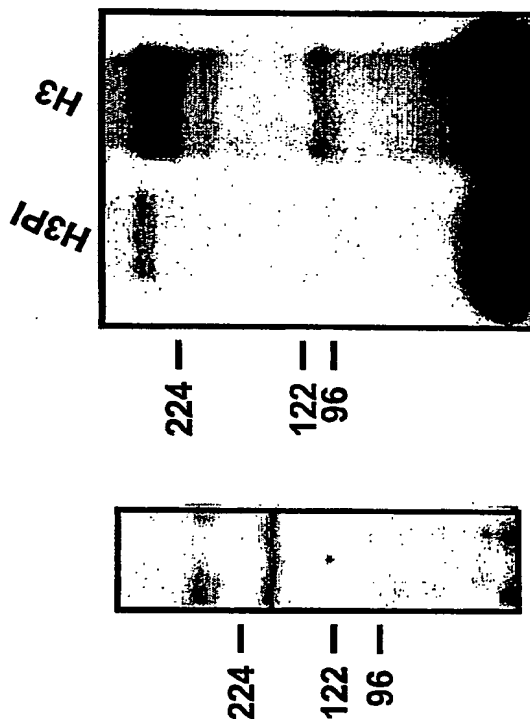
1 % TX-100

Calyculin A

NaF, NaPyrophosphate, NaVO3

Protease Inhibitor

IP: α -Homer 3 ab



Cerebellum

Buffer:

1 % CHAPS

Calyculin A

NaF, NaPyrophosphate, NaVO3

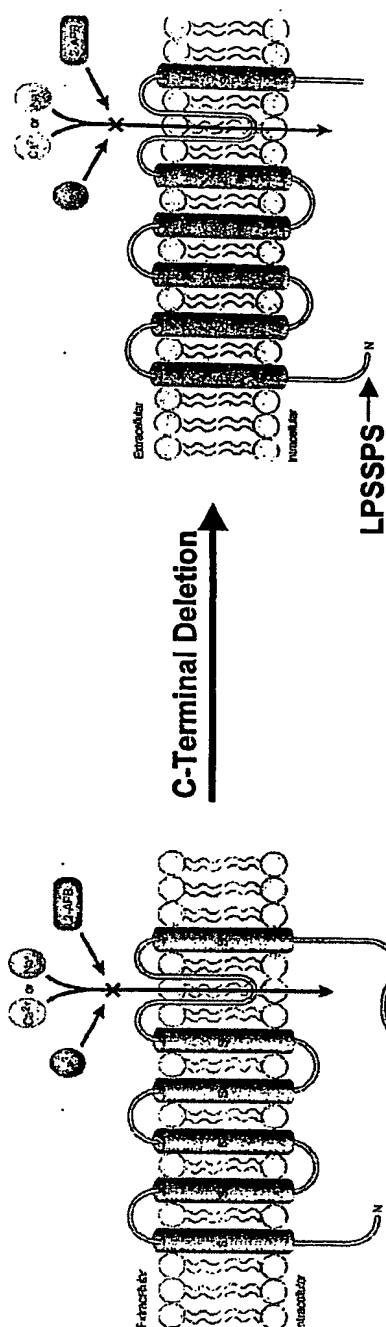
Protease Inhibitor

IB: α -TRPC1 ab

FIGURE 11

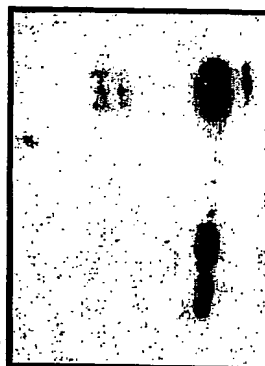
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Deletion of TRPC1 C-Terminus Reveals A Novel Homer Binding Site at the N-Terminus



GLUR1
TRPC1 NT
L19A
P20A
P23A
P28A

Homer3-GS⁺



Offered

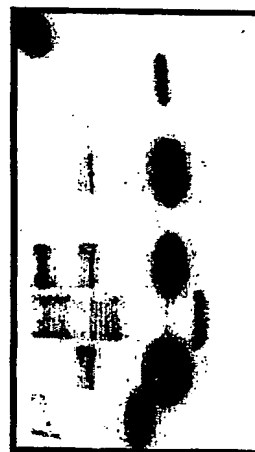


GLUR1
TRPC1 wt
Δ650-760
P645L
P646L
F648R
mGLUR5

Homer3-GST



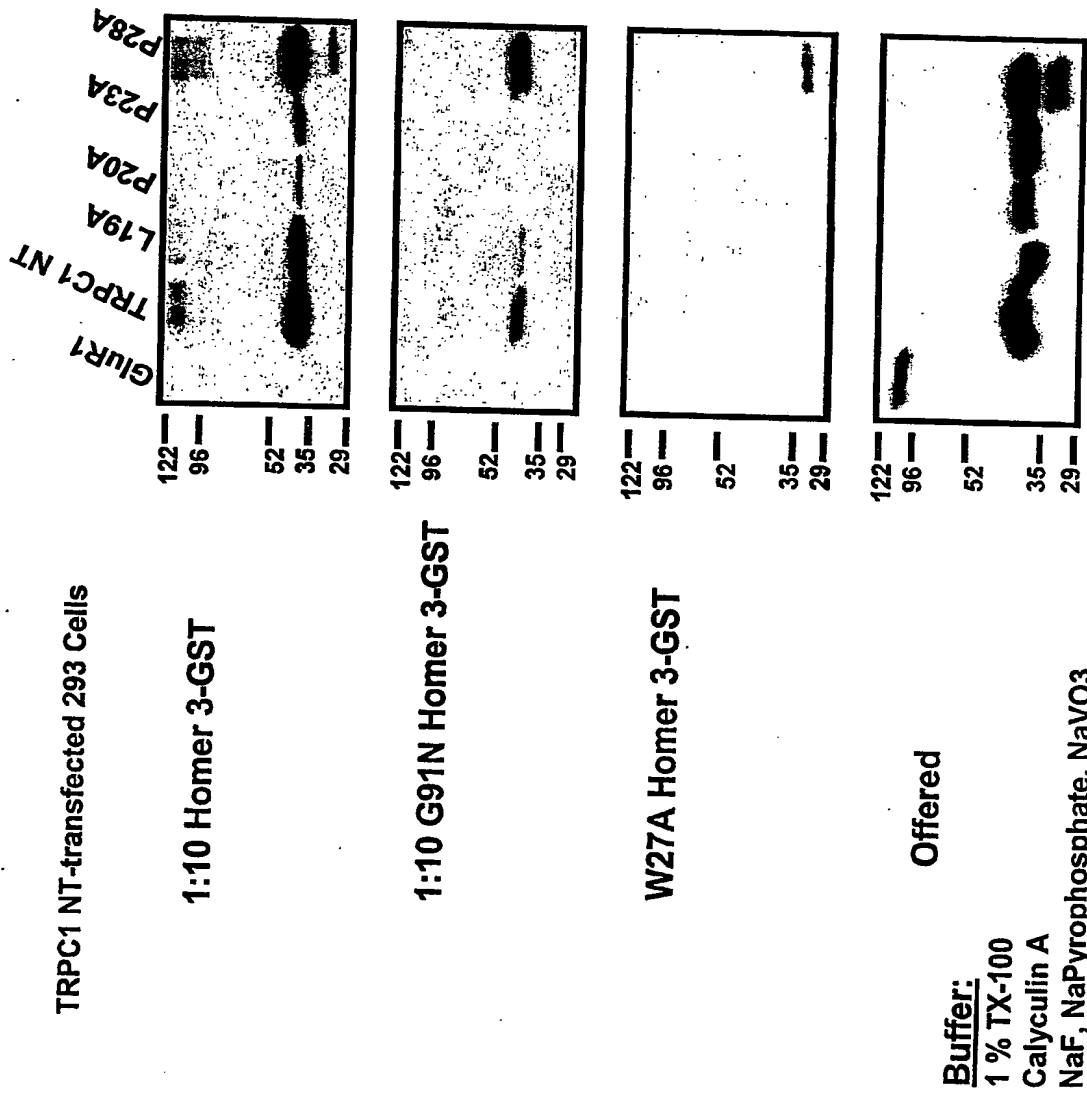
Offered



IB: α-HA ab (TRPC1)

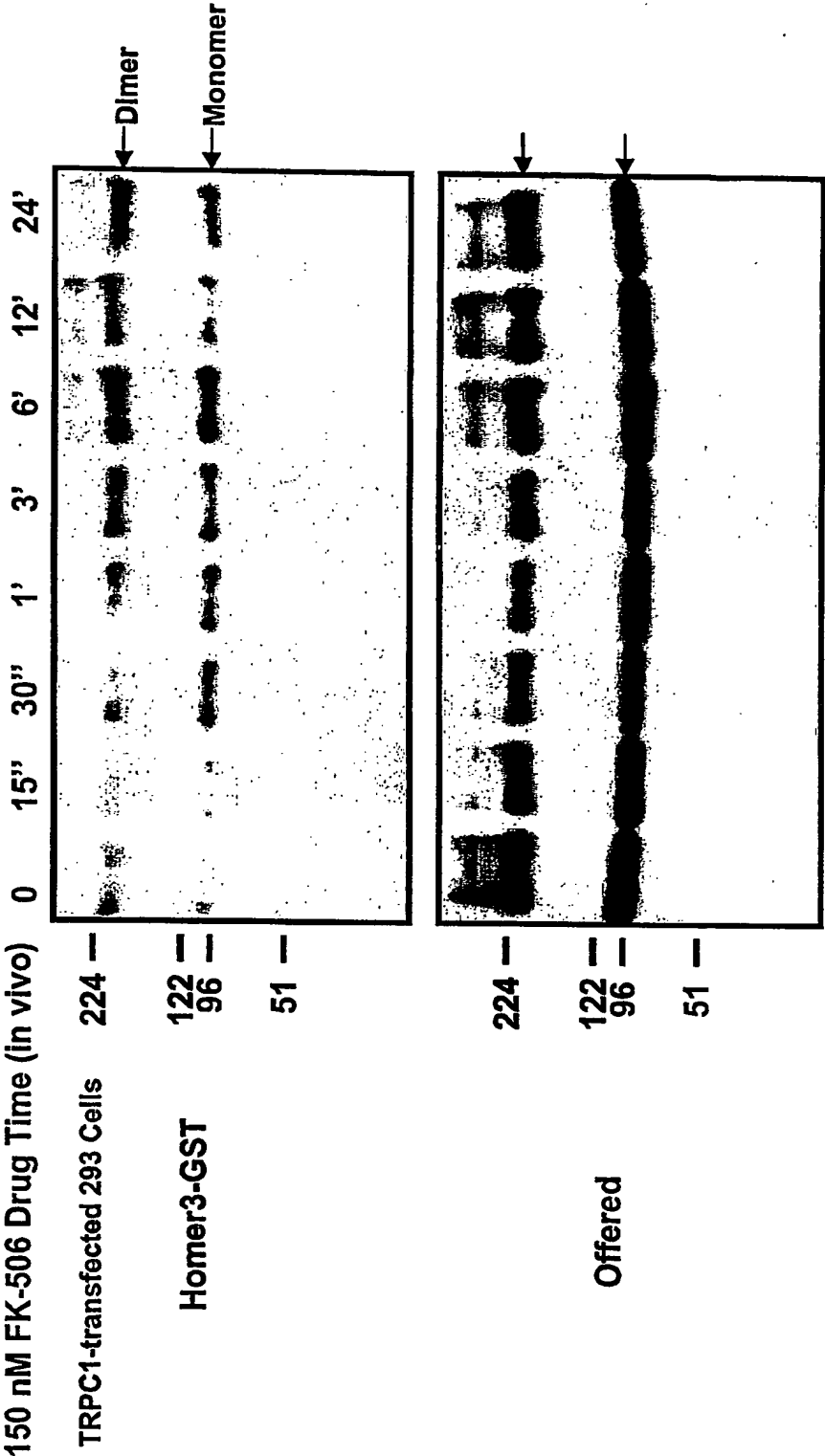
FIGURE 12

**WT and G91N Homer-GST Binds To
LPSSP Motif of TRPC1 N-Terminus**



Effect of FK-506 on TRPC1 Binding to Homer

Time Course



Buffer:
1 % TX-100
Calyculin A
NaF, NaPyrophosphate, NaVO3
Protease Inhibitor

FIGURE 14

Effect of Various Drugs on TRPC1 Binding to FKBP52

Dosage Dependence

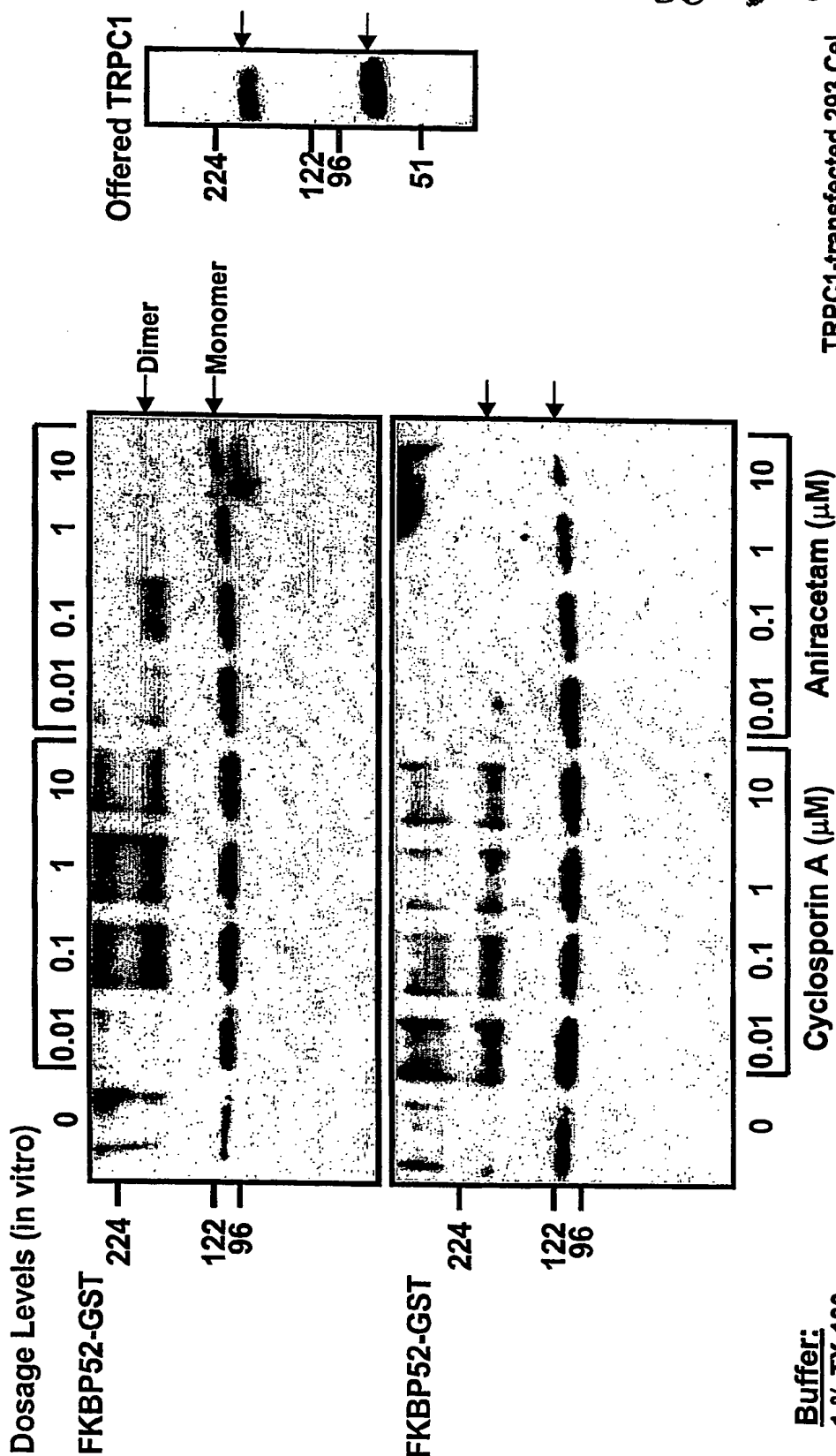


FIGURE 15

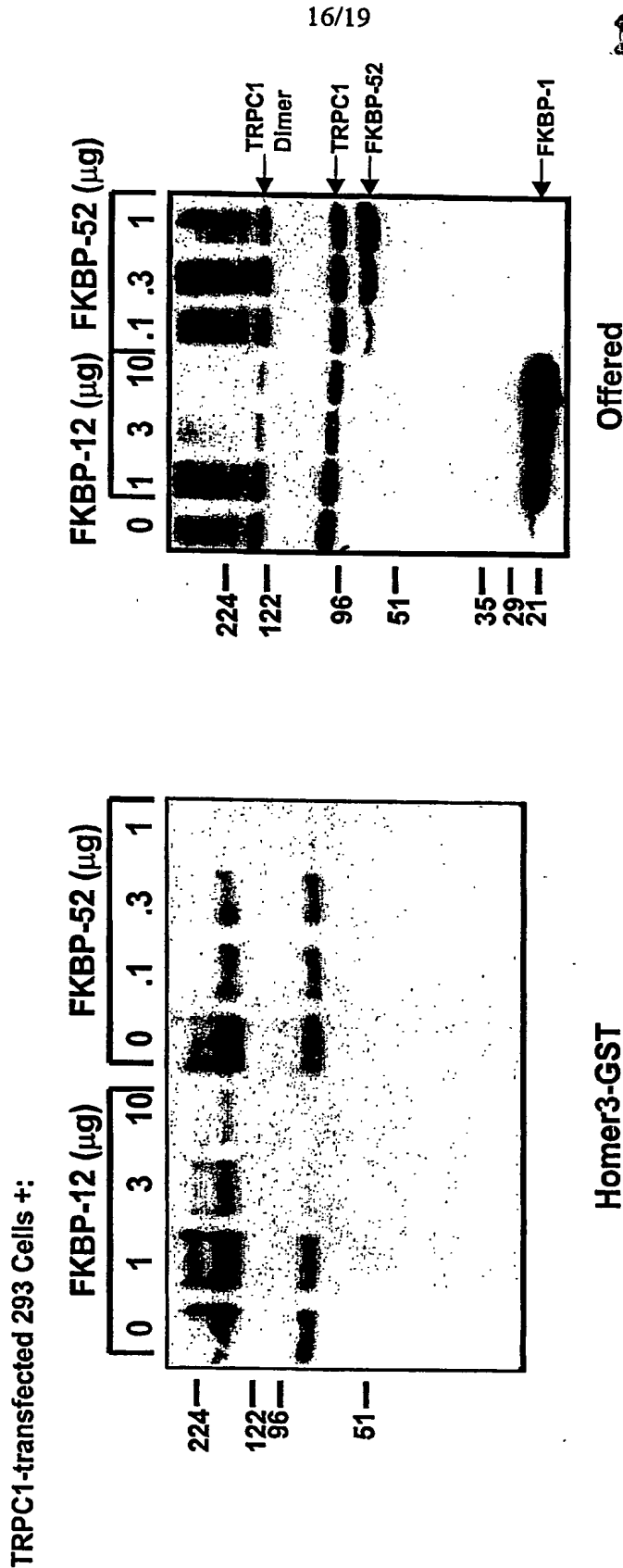
Effect of FKBP-12/FKBP-52 on TRPC1 Binding to Homer

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Buffer:

1 % TX-100

Calyculin A

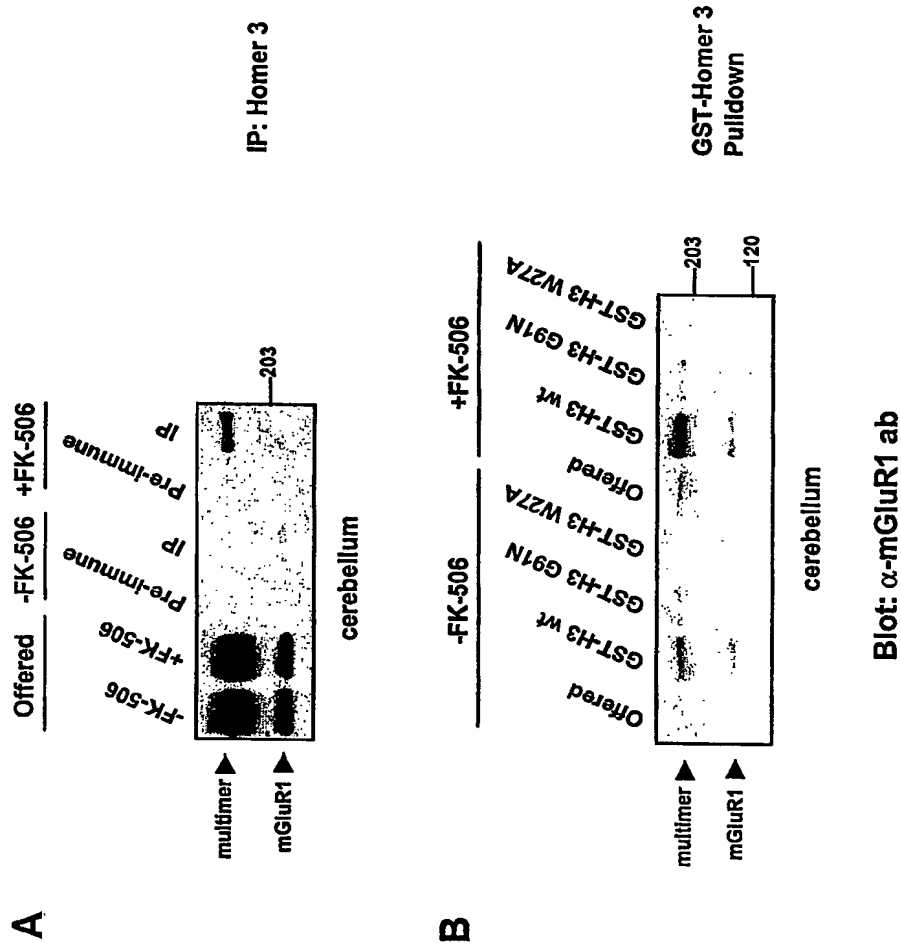
NaF, NaPyrophosphate, NaVO3

Protease Inhibitor

IB: α-HA 3b (TRPC1)

FIGURE 16

Effect of FK-506 on Homer-mGluR1 interaction *in vivo*



Adult rat was injected (i.p.) with 10 mg/kg FK-506 or vehicle only (DMSO). After 3 hours, the rats were sacrificed, and the cerebellum was collected. (A) Homer 3 co-immunoprecipitation of mGluR1 multimer increases with FK-506 treatment vs. control. (B) WT GST-Homer 3 pulldown of mGluR1 multimer increases with FK-506 treatment vs. control.

FIGURE 17

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atg ggg gaa caa cct atc ttc agc act cga gct cat gtc ttc cag atc
gac cca aac aca aag aag aac tgg gta ccc acc agc aag cat gca gtt
act gtg tct tat ttc tat gac agc aca agg aat gtg tat agg ata atc
agt cta gac ggc tca aag gca ata ata aat agc acc atc act cca aac
atg aca ttt act aaa aca tct caa aag ttt ggc caa tgg gct gat agc
cgg gca aac act gtt tat gga ctg gga ttc tcc tct gag cat cat ctc
tca aaa ttt gca gaa aag ttt cag gaa ttt aaa gaa gct gct cgg ctg
gca aag gag aag tcg cag gag aag atg gaa ctg acc agt acc cct tca
cag gaa tca gca gga gga gat ctt cag tct cct tta aca cca gaa agt
atc aat ggg aca gat gat gag aga aca ccc gat gtg aca cag aac tca
gag cca agg gct gag cca gct cag aat gca ttg cca ttt tca cat agg
tac aca ttc aat tca gca atc atg att aaa

Figure 18

Met Gly Glu Gln Pro Ile Phe Ser Thr Arg Ala His Val Phe Gln Ile
Asp Pro Asn Thr Lys Lys Asn Trp Val Pro Thr Ser Lys His Ala Val
Thr Val Ser Tyr Phe Tyr Asp Ser Thr Arg Asn Val Tyr Arg Ile Ile
Ser Leu Asp Gly Ser Lys Ala Ile Ile Asn Ser Thr Ile Thr Pro Asn
Met Thr Phe Thr Lys Thr Ser Gln Lys Phe Gly Gln Trp Ala Asp Ser
Arg Ala Asn Thr Val Tyr Gly Leu Gly Phe Ser Ser Glu His His Leu
Ser Lys Phe Ala Glu Lys Phe Gln Glu Phe Lys Glu Ala Ala Arg Leu
Ala Lys Glu Lys Ser Gln Glu Lys Met Glu Leu Thr Ser Thr Pro Ser
Gln Glu Ser Ala Gly Gly Asp Leu Gln Ser Pro Leu Thr Pro Glu Ser
Ile Asn Gly Thr Asp Asp Glu Arg Thr Pro Asp Val Thr Gln Asn Ser
Glu Pro Arg Ala Glu Pro Ala Gln Asn Ala Leu Pro Phe Ser His Arg
Tyr Thr Phe Asn Ser Ala Ile Met Ile Lys

Figure 19

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